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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/622,452

10/31/2000

David B. Weiner

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EXAMINER

WEHBE, ANNE MARIE SABRINA

ART UNIT

PAPER NUMBER

1633

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/622,452	Applicant(s) WEINER ET AL.	
	Examiner Anne Marie S. Wehbe	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4,6,7,9-12,15,17,18,33,36,42-44 and 46-55 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4,6,7,9-12,15,17,18,33,36,42-44 and 46-55 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/31/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/07 and the accompanying amendment and response have been entered. Claims 2-3, 5, 8, 13-14, 16, 19-32, 34-35, 37-41, and 45 are canceled and new claims 53-55 have been added. Claims 1, 4, 6-7, 9-12, 15, 17-18, 33, 36, 42-44, and 46-55 are currently pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Claim Objections

The objection to pending claims 1, 4, 6-7, 9-12, 15, 17-18, 33, 36, 42-44, and 46-55 for continuing to recite non-elected subject matter, there being no allowable generic claim, is maintained. The applicant argues that all the claims recite the elected species and that once this species is found to be allowable that the generic claims and a reasonable number of non-elected species be examined and allowed. In response, it is first noted that the instant claims have not

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been found allowable based on examination of the elected species of DR5. Further, MPEP

809.02(a) states:

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

The generic claims have also not been found allowable, thus consideration of non-elected species is not required. Thus, the objection to the claims remains.

Claim Rejections - 35 USC 112

The rejection of claims 1-4, 6-7, 9-15, 17-18, 33-36, 40-45, 47-48, and 50-52 under 35 U.S.C. 112, first paragraph, for scope of enablement is maintained over currently pending claims 1, 4, 6-7, 9-12, 15, 17-18, 33, 36, 42-44, and 46-55. Applicant's amendments and arguments have been fully considered but have not found persuasive in overcoming the grounds of rejection for reasons of record as discussed in detail below.

The applicant argues that since the claims have been amended to recite that the antigen is a pathogen antigen and that therefore the claims no longer read on cancer or auto-immune antigens that the rejection should be withdrawn. In response, the limitation of the claims to a "pathogen" antigen does not overcome this scope of enablement rejection. The previous office actions stated that the specification, while being enabling for 1) a method of immunizing a mammal against Influenza comprising co-administering a plasmid DNA encoding Influenza HA and a plasmid encoding DR5 by intramuscular injection and 2) a pharmaceutical composition

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comprising a plasmid encoding Influenza HA and a plasmid encoding DR5, does not reasonably provide enablement for pharmaceutical compositions comprising a plasmid encoding any immunogen and a plasmid encoding DR5 or for methods of enhancing an immune response or methods of immunizing against any pathogen by administering plasmid(s) encoding an immunogen and DR5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Please note that while claims 1-4, 6, 9-10, 12-15, 17, 40, and 42-43 are composition or pharmaceutical composition claims, they have been included in this rejection based on the disclosed intended use of the compositions for immunizing a host against disease. Thus, it can be seen from the previously identified scope of enablement, that the lack of enablement was not limited to cancer antigens and autoimmune antigens. The rejection of record provides a detailed analysis of why the specification does not provide an enabling disclosure for methods of enhancing an immune response or methods of immunizing against any pathogen by administering plasmid(s) encoding any pathogen immunogen and DR5, or for pharmaceutical compositions comprising plasmid(s) encoding any pathogen immunogen and DR5.

The applicant further argues that all method claims have previously been amended to recite the use of intramuscular injection, and that the evidence of record supports the enablement of the invention as claimed. In response, as noted in the previous office action, while applicant's amendments of the method claims to limit the route of administration to intramuscular overcomes one issue regarding the lack of enablement for the methods and compositions as broadly claimed, numerous issues remain that are not addressed by this limitation, such as the lack of enablement for generating therapeutic immune responses to any pathogen antigen using

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the claimed compositions/pharmaceutical compositions other than the generation of a therapeutic CTL response against Influenza by co-administering a plasmid DNA encoding Influenza HA and a plasmid encoding DR5 by intramuscular injection. Furthermore, the finding for lack of enablement for the full scope of the claimed invention was determined by a full and careful consideration of all the evidence of record, including the teachings of the specification, the Declaration under 37 CFR 1.132 by David Weiner, and the state of the art at the time of filing. It is further noted that the previous office actions analyzed the specification in direct accordance to the factors outlined in *In re Wands*, namely 1) the nature of the invention, 2) the state of the prior art, 3) the predictability of the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of the skilled artisan, and 8) the breadth of the claims, and presented detailed scientific reasons for the finding of a lack of enablement for invention as claimed. It is also noted that case law including the Marzocchi decision sanctions both the use of sound scientific reasoning and printed publications to support a holding of non-enablement (see *In re Marzocchi* 169 USPQ 367, and *Ex parte Sudilovsky* 21 USPQ2d 1702). Further, the unpredictability of a particular art area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See *Ex parte Singh*, 17 USPQ2d 1714 (BPAI 1991). 35 U.S.C. 112 also requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970).

In particular, the previous office action stated that while the applicant's Declaration provides evidence that DR5 can act to increase HA specific CD8⁺ T cells when co-administered

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to muscle with the antigen in the form of plasmid DNA, the declaratory evidence is not commensurate in scope with the breadth of the instant claims as written. Claims 33 and 55 continue to broadly claim the administration of any nucleic acid molecule, rather than a plasmid or plasmid(s). The cited art of record demonstrates that the type of immune response generated is affected by the route of administration and delivery vehicle (see Abbas et al. and Golding et al.). Further, the remaining method claims continue to read broadly on immunizing an individual against any pathogen or against herpes simplex virus or influenza. The manuscript provided with the last response as Exhibit 1 does not teach or suggest that the co-administration of plasmid encoding DR5 has any effect on B cell responses, or any other immune effector cell responses other than CD8⁺ T cell responses, and the prior art of record teaches that the generation of antigen specific CD8⁺ T cells does not predictably correlate with a treatment effect on viral infections (see Yasutomi et al., Erdile et al., and Ertl et al.). It is further noted that while the declaratory evidence did in fact demonstrate a correlation between the generation of Influenza HA specific CTL by intramuscular injection of plasmid encoding HA and DR5, no such correlation was demonstrated for HIV antigen specific CTL and the cited prior art of record clearly teaches that immunization against HIV was considered highly unpredictable at the time of filing (see Fox, and Klein et al.).

Therefore, in view of the state of the art of generating therapeutic immune responses at the time of filing, the lack of specific guidance provided by the specification for using DR5 to enhance immune responses, the limitation of the declaratory evidence to a showing that DR5 can enhance CD8⁺ T cell responses to Influenza antigens using intramuscular injection, the art recognized unpredictability in immunizing against any pathogenic disease by generating a CD8⁺

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T cell response, and the breadth of the claims, it would have required undue experimentation to practice the scope of the invention as claimed.

Claim Rejections - 35 USC 102

The rejection of previously pending claims 1-3, 6, and 12 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,417,328 (7/9/02), hereafter referred to as Alnemri, is maintained over claims 1, 6, 12, and 53-54, claims 2-3 having been canceled. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection of record for reasons of record as discussed in detail below..

The applicant reiterates their previous argument that Alnemri et al. does not teach a "pyrogen free" composition, and that while Alnemri teaches "expressible nucleic acids encoding DR5", the current claims recite a plasmid comprising a nucleic acid encoding DR5 and not an "expressible nucleic acid encoding DR5". In response, Alnemri et al. clearly teaches a plasmid encoding DR5 and the immunogen LacZ, which is a bacterial antigen, or the combination of the plasmid encoding DR5 and the plasmid encoding CrmA, a viral protein antigen, and further provides teachings for making a sterile aqueous solution in columns 22-23. The disclosure in column 22 concerning therapeutic compositions of DR5 does refer to "expressible nucleic acids encoding DR5". However, as stated in previous office actions, the plasmids exemplified in columns 27-28 are in fact expressible nucleic acids. Further, Alnemri broadly teaches to prepare "expressible nucleic acids encoding DR5" as sterile aqueous solutions that do not contain any material other than the nucleic acid and water or physiological saline (column 23, lines 12-17).

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As such, the teachings in columns 22-23 to prepare sterile aqueous solutions of the nucleic acids reads on the particular plasmids disclosed in the examples. Also, as stated in previous office actions, a sterile aqueous solution that does not contain any material other than the nucleic acid and water or physiological saline appears to qualify as "pyrogen-free" absent evidence to the contrary. Therefore, for reasons of record as discussed in detail above, the rejection stands.

Claim Rejections - 35 USC § 103

The rejection of previously pending claims 1-3, 6, and 12 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,417,328 (7/9/02), hereafter referred to as Alnemri, in view of U.S. Patent No. 5,693,622 (12/2/97), hereafter referred to as Wolff et al. is maintained over currently pending claims 1, 6, 12, and 53-54, claims 2-3 having been canceled.. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection of record for reasons of record as discussed in detail below.

The applicant reiterates their argument that there is no motivation to make a pyrogen free plasmid or composition in either Alnemri or Wolff, since neither references teaches or suggests the immuno-enhancing effects of DR5. These arguments have been addressed in full in the previous office actions, the relevant sections of which are included below.

In response, it is first noted that the claims under rejection are product claims. The fact that applicant has recognized another advantage which would flow naturally from following the teachings and suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App.

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& Inter. 1985). Also, as discussed in detail above, since the Alnemri specification broadly teaches to prepare “expressible nucleic acids encoding DR5” as sterile aqueous solutions that do not contain any material other than the nucleic acid, water or physiological saline, the teachings in column 22 to prepare sterile aqueous solutions of the nucleic acids reads on the particular plasmids disclosed in the examples, which include a single plasmid encoding DR5 and the bacterial pathogen immunogen LacZ or the combination of a plasmid encoding DR5 and a plasmid encoding CrmA, a viral pathogen antigen, regardless of whether they were actually used in *in vitro* experiments versus *in vivo* methods. Thus, in view of teachings of Alnemri et al. to prepare a sterile pharmaceutical composition comprising a plasmid(s) encoding DR5 for administration to a mammal, and the teachings of Wolff et al. for standard methods of preparing plasmid DNA for *in vivo* administration, it would have been *prima facie* obvious to the skilled artisan at the time of filing to use the standard methods taught by Wolff et al. to prepare the plasmids encoding DR5 and an immunogen taught by Alnemri et al.. Further, based on the standard nature of cesium chloride purification, and the high level of skill in the art of molecular biology at the time of filing, the skilled artisan would have had a reasonable expectation of success in producing a pyrogen-free composition containing the plasmid(s) taught by Alnemri et al. using the purification method taught by Wolff et al. Finally, regarding applicant’s argument that the use of DR5 results in an “unexpected result” of enhanced immune response, it is reiterated that the claims under rejection are simply product claims, not method claims, and the references need to provide the same motivation for making the plasmid(s) as applicant. Therefore, the rejection of record is maintained.

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology

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center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/

Primary Examiner, A.U. 1633